REMARKS

Claims 1-14, 17-19, 42, 50 and 57 are pending in the instant application. Applicants' have amended claims 8, 10, and 19 to further clarify the claims. Claims 8 and 10 were amended merely to place the claims in a more suitable form, and Claim 19 was amended to further clarify the claim. No new matter has been added by these amendments which are fully supported by the specification and claims as originally filed. Entry of the amendments and the remarks made herein into the record for the above-identified application is respectfully requested.

The present invention relates to an implantable device that mimics the activity of a lymph node in order to modulate the immune response in a mammal to an antigen. (Page 13, Lines 17-18). Lymph nodes are bean-shaped organs that contain a large number of leukocytes embedded within a matrix of fibrous tissues. The lymph nodes assist in the body's immune system by filtering out infectious and toxic agents and producing antibodies to these foreign agents. The efficacy of this organ is in part due to the high concentration of agents that accumulate within the lymph node and of lymphocytes and macrophages present within the device.

The present invention replicates this environment within a novel implant made of a porous matrix impregnated or injected with the antigen contained within a perforated but otherwise impermeable container. (Page 4, Lines 12-15). The container acts as a diffusion barrier: maintaining within the device high levels of cytokines and other co-stimulatory factors produced by immune cells attracted to the device which in turn enhance the response of subsequent immune cells attracted to the device. (Page 4, Line 21 to Page 5, Line 1). Thus, the diffusion barrier generated by the perforated but otherwise impermeable container permits the device to produce an immune response to the antigen similar to that generated by the lymph nodes with the body. (Page 12, Lines 3-6).

THE REJECTIONS UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claims 1-3, 7, 8, 10, 12, 13, 50 and 57 are rejected as being anticipated by U.S. Patent No. 4,689,220 to Sturmer et al. ("Sturmer et al."). The Office Action claims that Sturmer et al. discloses the induction of an immune response through the implantation of an antigen impregnated substrate. It further argues that the container and matrix presently claimed are one in the same.

Applicants argue that the matrix and container of the presently claimed device are not one in the same and, further, that Sturmer et al. fails to anticipate the presently claimed device since it lacks the diffusion barrier provided by the perforated impervious container of the present invention.

First, within the presently claimed device the matrix and the container serve different purposes. The porous matrix, *i.e.*, a sponge-like material, of the device acts as a depository for the antigen. The antigen can either be incorporated into the matrix or injected into the matrix prior to or after implantation. (Page 19, line 21 to Page 20, Line 12). The container, however, is a perforated impervious coating surrounding the matrix that acts as a diffusion barrier. (Page 20, Line 13 to Page 23, Line 7). The container is less porous than the matrix having a limited number of perforations, optimally about 10 per centimeter, to achieve a balance between permitting the active recruitment of immune cells into the device while preventing the passive diffusion of antigens and small molecules such as co-stimulatory factors (cytokines produced by immune cells within the device) out of the device. The device of the present invention generates a robust immune response since subsequent immune cells are primed when they come into contact with the antibody of interest or the various small molecules concentrated within the device. The diffusion barrier of the device optimizes the development of an immune response to the antigen by maintaining a high concentration of antigens and small molecules within the device and this also imparts long-term immunity by producing a population of memory cells. Thus, the matrix and the container of the present device are not one in the same.

Sturmer et al. discloses an immunogenic implant consisting of a porous biologically-compatible substrate impregnated with the antigen of interest. (Col. 2, Lines 30-37). The immunogenic implant tanght by Sturmer et al. does not incorporate a perforated impermeable container, let alone a diffusion barrier. Although Sturmer et al. teaches that the antigen of interest should be secured to the matrix to prevent the antigen from seeping into the surrounding tissue (col. 2, lines 54-56), it does not teach the use of a diffusion barrier to also prevent cytokines and other factors secreted by immune cells within the implant from seeping into the surrounding tissues. Therefore, the immunogenic implant taught by Sturmer et al. does not anticipate the device for modulating the immune response taught by the present invention.

Claims 1, 2, 6-10, 12, 13, 50 and 57 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,538,733 to Emery et al. ("Emery et al."). According to the

Office Action, Emery et al. teaches the use of an implant comprised of a polylactide substrate that contains an immunogenic agent to prime an immune response. Once again, the Office Action argues that the matrix and the container are one and the same, and therefore Emery et al. anticipates the device claimed in the present application.

For the reasons stated above, the Applicants dispute the assertion that the matrix and the container disclosed within the present invention are the same.

Furthermore, Emery et al. does not anticipate the perforated impermeable container/diffusion barrier of the present invention. Emery et al. discloses an implant comprised of biocompatible, biodegradable, bioabsorbable and/or bioerodible polymeric material that will release an immunogenic agent for sustained delivery into the surrounding tissue fluids. (Col. 2, Line 15-37). According to the Emery et al. this priming dose of the immunogenic agent is maintained within the circulatory system of the animal by its release from the implant into the tissue fluids of a young animal. *Id.* Emery et al. teaches the release of antigens into the surrounding tissues as opposed to retaining a concentration of antigens within the device, and therefore the use of a diffusion barrier would be contrary to the aims of the Emery implant. However, in the implant of the present invention, "the antigen is retained within the device and its concentration remains high, as do the concentrations of co-stimulatory factors secreted by the cell population with[in] the device, much in the same fashion as within a lymph node." (Page 14, Lines 20-22) The present invention utilizes the perforated impermeable container/diffusion barrier to limit the passive diffusion of the antigens out of the device and thereby maintain a high concentration of antigens and small molecules within the device. Thus, Emery et al. does not disclose the use of a perforated impermeable container/diffusion barrier within the device and fails to anticipate the presently claimed invention.

Accordingly, applicants respectfully submit that the 35 U.S.C. § 102 rejections for anticipation in light of Sturmer et al. and Emery et al. have been overcome and request their withdrawal.

THE REJECTION UNDER 35 U.S.C. § 103 SHOULD BE WITHDRAWN

Claims 1-4, 6-10, 12, 13, 17-19, 50, 57 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Emery et al. in view of U.S. Patent No. 5,593,697 to Barr et al. ("Barr et al.") According to the Office Action, Barr et al. teaches the use of an implant to

release an active ingredient, such as an antigen, in pulses. Thus, the Office Action claims that it would have been obvious, in light of the Emery and Barr Patents, to use the vehicle of Barr et al. and the method of the Emery et al. to achieve the benefit of one administration of the implant.

Barr et al. discloses a single dose vaccination system in which an implant is provided that has an exterior insoluble film, an interior soluble film and a core containing the active ingredient and both soluble and insoluble excipients. (Col. 3, Line 13 to Col. 4, Line 14). According to Barr et al., the exterior film controls access of physiological fluid to the interior film. When physiological fluid reaches the interior film, the insoluble excipient begins to swell causing the failure of the exterior film and, consequently, the release of the active ingredient as a pulse. Given that Barr et al. discloses the release of antigen from the device, a diffusion barrier would be contrary to the aims of the Barr implant, and therefore Barr et al. does not teach the use of a diffusion barrier.

Thus, the Applicants maintain that the present invention is novel and non-obvious even in light of the suggested combination of Emery et al. and Barr et al. since neither teaches the use of a perforated impermeable container/diffusion barrier. Specifically, the present invention teaches the importance of maintaining a high concentration of antigens and small molecules within the implant. The present invention incorporates a perforated but otherwise impermeable container as a diffusion barrier to maintain the concentration of antigens and small molecules within the implant. Neither Emery et al. nor Barr et al. disclose the need to maintain a high concentration of antigens within their respective devices. On the contrary, both Emery et al. and Barr et al. teach the release of antigens from the device, and therefore fail to disclose the use of a perforated but otherwise impermeable container since it would interfere with the release of the antigen.

Accordingly, Applicants respectfully submit that the 35 U.S.C. § 103 rejection for anticipation in light of Emery et al. and Barr et al. has been overcome and requests its withdrawal.

THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH SHOULD BE WITHDRAWN

Claims 8, 10, and 19 were rejected as being indefinite under 35 U.S.C § 112, second paragraph. Specifically, the Office Action claimed that it was unclear whether a Markush

group was intended within claims 8 and 10. Additionally, the Office Action noted that the term "Reintroduced into" appeared to contradict the presence of sufficient antigen within the device.

As noted, the Applicants have amended claims 8, 10, and 19 in order to further clarify the subject matter of these claims. Applicants believe that these amendments overcome the indefiniteness objections.

CONCLUSIONS

Applicants respectfully request that the foregoing amendments and remarks be made of record in the file history of the instant application. Applicants estimate that the remarks and amendments made herein now place the pending claims in condition for allowance.

Respectfully submitted,

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